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Subject: Environmental Defense comments on Chloromethyl Methyl Ether (CAS# 107-30-2)

(Submitted via Internet 6/24/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and kdnitsch@dow.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Chloromethyl Methyl Ether (CAS# 107-30-2).

The test plan and robust summaries for chloromethyl methyl ether (CMME) were submitted by Dow Chemical Company. The sponsor considers this test plan incomplete and plans to submit a final version later, although no date for completion was indicated. The sponsor states in the executive summary that a consortium is being formed with other producers of CMME to better document the uses and exposure conditions for this chemical. We applaud the sponsor for establishing the consortium, since this is a very toxic chemical and it will be important to make available all data relevant to environmental and human exposures. However, the consortium should have been established sooner so that the deadline for submission could have been met.

CMME is a known human carcinogen based on numerous epidemiology studies in workers and several experimental animal studies. The lung and respiratory tract were the primary sites for cancer, and the studies are well-described in the robust summaries. In addition, there is a 30-day repeat dose study in rats so the repeat dose toxicity endpoint has been more than met. However, we do ask the sponsor, in the revised submission, to provide a summary of the histological methods used in the repeat dose and cancer studies.

The test plan indicates that no reproductive or developmental studies are available on CMME, but the sponsor does not indicate whether or not such studies will be performed. Studies for such endpoints are required, and we recommend that the sponsor conduct a combined reproductive/developmental toxicity study via the inhalation route of exposure. It would be helpful also to provide information on reproductive tract histology from interim sacrifices, if available, from the cancer studies.

The test plan also notes that no data are available for the ecological toxicity endpoints: toxicity to fish, aquatic invertebrates and algae. The sponsor contends that these studies are not needed because CMME is highly reactive and rapidly hydrolyzed. The degradation products include formaldehyde, methanol and hydrochloric acid, and all of these have data for the three ecological toxicity endpoints. If formaldehyde, methanol and hydrochloric acid constitute the great majority (e.g., at least 90%) of the total hydrolysis products, then we can agree with the sponsor. If other degradation products occur in significant amounts and are not themselves derived from formaldehyde, methanol or hydrochloric acid, then it may be necessary to conduct the aquatic toxicity tests. Therefore, we request that additional information on hydrolysis/degradation products be provided in the revised test plan submission.

Other comments are as follows:

1. The TLV-TWA in the workplace for CMME is 1 ppb, and the sponsor states that protective devices are worn by workers. This is important since CMME is such a potent carcinogen and the allowable workplace levels may be too high. Are monitoring data available which (hopefully) demonstrate that workplace levels are consistently below 1 ppb?

2. The test plan summary on in vitro mutagenicity is inconsistent with the information provided in the robust summaries. The test plan states that only one in vitro test was positive. However, the robust summaries indicate that there are at least four positive tests for mutation, DNA damage and repair and chromosomal aberrations. Also, the heading for the section on in vivo tests in the robust summaries incorrectly reads "in vitro."

3. Although CMME is rapidly hydrolyzed in water, it is more stable in air, with a half-life that can be as high as several days. Are the same degradation products formed in air as in water, but at a slower rate in air? Are the degradation products responsible for the carcinogenicity of CMME following inhalation exposures, and/or is the inherent reactivity of CMME the primary mode of action?

4. There are several other typographical errors that need to be corrected in the revised submission.

Thank you for this opportunity to comment.

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